

CLAIMS

1. A polynucleotide comprising at least two repeats of a hypoxia response element (HRE), wherein the hypoxia-inducible factor (HIF) consensus binding sites within each of the two repeats are separated by a spacer of at least 20 contiguous nucleotides.
2. A polynucleotide according to claim 1 wherein the HRE repeats are operably linked to a viral promoter.
3. A polynucleotide according to claim 1 or 2 wherein said spacer comprises a nucleotide sequence as shown in SEQ I.D. No. 10 or SEQ I.D. No. 11.
4. A polynucleotide according to claim 2 or 3 wherein said promoter is selected from an SV40 promoter or an MLV promoter.
5. A polynucleotide according to any one of the preceding claims comprising at least two repeats of the HRE operably linked to the promoter and upstream (5' to) the promoter and at least two repeats of the HRE operably linked to the promoter and downstream (3' to) the promoter.
6. A polynucleotide comprising at least three repeats of a phosphoglycerate kinase (PGK) hypoxia response element (HRE) operably linked to an SV40 promoter or an MLV promoter.
7. A polynucleotide according to claim 6 comprising at least three repeats of the HRE operably linked to the promoter and upstream (5' to) the promoter and at least three repeats of the HRE operably linked to the promoter and downstream (3' to) the promoter.
8. A polynucleotide according to any one of the preceding claims wherein the HRE repeats are direct repeats.

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9. A polynucleotide according to any one of the preceding claims wherein the HRE comprises a nucleotide sequence as shown in SEQ I.D. No. 1 or SEQ I.D. No. 2.
10. A polynucleotide according to claim 1 comprising a nucleotide sequence as shown in SEQ I.D. No. 9.
11. A polynucleotide according to claim 6 comprising a nucleotide sequence as shown in SEQ ID. No. 3, SEQ ID. No. 4 or SEQ ID. No. 5.
12. A polynucleotide according to any one of the preceding claims operably linked to a nucleic acid of interest (NOI) such that the polynucleotide directs expression of the NOI in a host cell.
13. A polynucleotide according to claim 12 wherein the NOI encodes HIF-1.
14. A polynucleotide according to claim 13 wherein the promoter lacks a CAAT box sequence.
15. A polynucleotide according to any one of claims 12 to 14 wherein the host cell is a tumour cell.
16. A polynucleotide according to claim 12 wherein the NOI encodes a polypeptide of therapeutic use.
17. A polynucleotide according to claim 12 wherein the NOI encodes a polypeptide which is cytotoxic.
18. A polynucleotide according to claim 12 wherein the NOI encodes a polypeptide capable of converting a precursor prodrug into a cytotoxic compound.
19. A polynucleotide according to any one of claims 15 to 18 wherein the NOI is selected from polynucleotide sequences encoding proteins involved in the regulation of cell

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division, enzymes involved in cellular metabolic pathways, transcription factors and heat shock proteins.

20. A polynucleotide according to any one of claims 15 to 19 for use in delivering the NOI to a mammalian cell.
21. A nucleic acid vector comprising a polynucleotide as defined in any one of the preceding claims.
22. A viral vector comprising a polynucleotide as defined in any one of claims 1 to 20.
23. A viral vector according to claim 22 which further comprises a nucleotide sequence selected from (i) a nucleotide sequence encoding an inhibitory RNA molecule capable of effecting the cleavage, directly or indirectly, of VHL RNA; (ii) one or more inhibitory RNA molecules that bind to and prevent VHL RNA processing and/or expression; and (iii) a nucleotide sequence encoding a polypeptide capable of inhibiting the binding of VHL to Elongin B and/or Elongin C.
24. A viral vector according to claim 23 wherein said polypeptide is a non-functional derivative of wild type VHL.
25. A viral vector according to any one of claims 22 to 24 wherein the viral vector is a retroviral vector.
26. A viral vector according to any one of claims 22 to 24 wherein the viral vector is an adenoviral vector.
27. A viral vector according to claims 25 wherein the viral vector is a lentiviral vector.
28. A polynucleotide according to any one of claims 12 to 19, a nucleic acid vector according to claim 21 or a viral vector according to any one of claims 22 to 27 for use in a

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method of treatment of a human or animal patient suffering from a disease in which hypoxia is a cause or a symptom or is otherwise present.

29. A pharmaceutical composition comprising a polynucleotide according to any one of claims 12 to 19, a nucleic acid vector according to claim 21 or a viral vector according to any one of claims 22 to 27 together with a pharmaceutically acceptable carrier or diluent.

30. A method of treatment of a human or animal patient suffering from a disease in which hypoxia is a cause or a symptom or is otherwise present which method comprises administering an effective amount of a pharmaceutical composition according to claim 29 to the patient in need of such treatment.

31. A method of producing a viral strain which method comprises introducing a polynucleotide as defined in any one of claims 1 to 19 into the genome of a virus.

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